REMARKS

This Amendment, filed in reply to the Office Action dated April 29, 2010, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 1, 2, 4, 11-37 and 40-42 are all the claims pending in the Application. Claims 1, 11, 12 and 14-37 are withdrawn from consideration as allegedly being directed to non-elected inventions. Claims 2, 4, 13 and 40-42 are rejected. Claim 2 is amended herewith to recite the positive method step of "making a diagnosis that said patient has, or is susceptible to, open angle glaucoma when said subject has at least one polymorphism selected from the group consisting of an adenine at position 462 of the Noelin 2 gene and a cytosine at position 1105 of the Myocilin gene." Support for this amendment can be found throughout the specification as originally filed, and at, for example, page 10, lines 1-5, and page 19, 1st paragraph. Because original Claim 2 recited using a set of polymorphisms selected from the Markush group of Claim 1, and because Applicants elected a particular *species* of set in response to a requirement by the Office that a *species* of set from the Markush group be elected, this Amendment is fully responsive. *See* M.P.E.P. § 821.03. Further, Claim 13 is amended herewith to correct antecedent basis in view of the amendments to Claim 2.

No new matter is added by way of this amendment. Entry and consideration of this Amendment are respectfully requested.

Information Disclosure Statements

Applicants thank the Examiner for returning signed and initialed copies of the PTO Forms SB/08 that accompanied the Information Disclosure Statements filed September 15, 2006, and August 13, 2008, indicating consideration of the references therein.

Withdrawn Rejections

1. Applicants thank the Examiner for withdrawal of the rejection of Claims 2-6 and 13 under 35 U.S.C. § 112, second paragraph, as set forth in the Office Action mailed September 9, 2009.

2. Applicants thank the Examiner for withdrawal of the rejection of Claims 2-6 and 13 under 35 U.S.C. § 112, first paragraph, as set forth in the Office Action mailed September 9, 2009.

3. Applicants thank the Examiner for withdrawal of the rejection of Claims 2-6 and 13 under 35 U.S.C. § 103, as set forth in the Office Action mailed September 9, 2009.

Claims 2, 4, 13 and 40-42 are Definite Under 35 U.S.C. § 112, Second Paragraph

On page 3 of the Office Action, Claims 2, 4, 13 and 40-42 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

In making the rejection, the Examiner contends that Claims 2, 4, 13 and 40-42 are indefinite as allegedly omitting active steps necessary to perform the stated purpose of the method, citing M.P.E.P. § 2172.01. Specifically, the Examiner contends that these claims are rendered indefinite because they do not recite an active process step of diagnosing the patient with open angle glaucoma, or making a prediction of their susceptibility to open angle glaucoma.

Solely in the interest of advancing prosecution, and without acquiescing to the merits of the rejection, Claim 2 is amended herewith to recite the positive method step of "making a diagnosis that said patient has, or is susceptible to, open angle glaucoma when said subject has at least one polymorphism selected from the group consisting of an adenine at position 462 of the Noelin 2 gene and a cytosine at position 1105 of the Myocilin gene." Such an amendment is amply supported by the specification as originally filed, such as at, for example, page 10, lines 1-5, and page 19, 1st paragraph. Applicants respectfully submit that the amendments overcome the rejection.

Withdrawal of the rejection is respectfully requested.

Claims 2, 4, 13 and 40-42 are Patentable Under 35 U.S.C. § 103

On page 4 of the Office Action, Claims 2, 4, 13 and 40-42 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Umeda *et al.* and Mukhopadhyay *et al.*, each of record, in view of Mukhopadhyay *et al.* (*Molecular Vision,* 2002, 8:442-448).

In making the rejection, the Examiner asserts that Umeda *et al.* discloses PCR amplification and sequencing of the optineurin gene, particularly exons 4, 5, 6 and 16, to detect polymorphisms associated with open angle glaucoma. Specifically, the Examiner asserts that Umeda *et al.* discloses a heterozygous 412G>A substitution amongst several glaucoma patients, including primary open-angle glaucoma and normal tension glaucoma. From this, the Examiner contends that Umeda *et al.* discloses obtaining a biological sample from a human subject, and analyzing the sample to determine the nucleotide at position 412 of the optineurin gene, as claimed. However, the Examiner acknowledges that Umeda *et al.* does not disclose determining

the nucleotide at position 462 of the noelin 2 gene, or determining the nucleotide at position 1105 of the myocilin gene.

In an attempt to rectify such deficiencies, the Examiner cites to Mukhopadhyay *et al.* (*Molecular Vision*, 2004, 10:304-314; "Mukhopadhyay #1"), and Mukhopadhyay *et al.* (*Molecular Vision*, 2002, 8:442-448; "Mukhopadhyay #2"). The Examiner contends that Mukhopadhyay #1 discloses noelin-2 as a gene putatively associated with eye disorders, such as primary open angle glaucoma, because it is expressed in the eye and shares olfactomedin domains with myocilin, citing the Abstract. Moreover, the Examiner contends that Mukhopadhyay #2 discloses myocilin as a gene containing polymorphisms causally related to eye disorders, such as primary open angle glaucoma.

In view of the above references, the Examiner takes the position that those of ordinary skill in the art would readily have modified the method of Umeda *et al.*, in view of the disclosures of Mukhopadhyay #1 and Mukhopadhyay #2, to further determine the nucleotide at position 462 of the noelin 2 gene, and the nucleotide at position 1105 of the myocilin gene. The Examiner alleges that those of ordinary skill in the art would have possessed sufficient motivation to make such a combination, based on an asserted association in the art between mutations in these genes, and eye disorders.

While the Examiner acknowledges that none of the cited references actually disclose that position 462 of the noelin-2 gene may exhibit a G>A polymorphism, or that position 1105 of the myocilin gene may exhibit a T>C polymorphism, much less that these polymorphisms have any causal relationship with glaucoma, the Examiner takes the position that the wherein clause recited in Claim 2 does not actually limit the scope of the claims, such that merely sequencing the neolin-2 and myocilin genes would be sufficient to practice the claimed method; the

Examiner contends that those of ordinary skill in the art, in addition to detecting the polymorphism at position 412 of the optineurin gene, would readily have sequenced the neolin-2 and myocilin genes to identity mutations associated with eye disorders, and in doing so, would have identified the nucleotides at positions 462 and 1105, respectively.

Applicants respectfully disagree, and traverse the rejection in view of the following remarks.

Initially, and without acquiescing to the merits of the rejection, Applicants respectfully point out that Claim 2 is amended herewith to recite the positive method step of "making a diagnosis that said patient has, or is susceptible to, open angle glaucoma when said subject has at least one polymorphism selected from the group consisting of an adenine at position 462 of the Noelin 2 gene and a cytosine at position 1105 of the Myocilin gene." Accordingly, even assuming *arguendo* that those of ordinary skill in the relevant field would have combined the reference disclosures in the manner asserted in the rejection, they would not have arrived at the presently claimed invention. Specifically, because no correlation between a polymorphism at position 462 of the noelin-2 gene or a polymorphism at position 1105 of the myocilin gene, and open-angle glaucoma, was recognized in the art at the time of the invention, those of ordinary skill in the art - even had they detected the recited polymorphisms by sequencing the entirety of these genes (as the rejection posits) - would not have possessed any reason to suspect that polymorphisms at these specific positions are associated with open angle glaucoma, or susceptibility thereto. It follows then, that those of ordinary skill in the art would not have possessed any reason or motivation to make a diagnosis of open angle glaucoma, or susceptibility thereto, based on the existence of these polymorphisms, much less possessed any expectation of success in doing so.

For the foregoing reasons, Applicants respectfully submit that the presently claimed invention is non-obvious, and patentable.

Withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

/Alan C. Townsley/

Alan C. Townsley, Ph.D.
Registration No. 64,740

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
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